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Outcome prediction in elderly aspiration pneumonia despite broad-spectrum antibiotic therapy Running title: Prognostic Score for Elderly Aspiration Pneumonia

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Abstract

In older patients with aspiration pneumonia, poor outcomes despite broad-spectrum antibiotic therapy may be more strongly associated with host vulnerability than with pathogen-related factors. This study aimed to develop and validate a prognostic score for in-hospital mortality in older patients with aspiration pneumonia receiving broad-spectrum antibiotics. We analyzed nationwide data from the Diagnosis Procedure Combination database for patients aged ≥ 65 years who were hospitalized with aspiration pneumonia in Japan between January and December 2018 and received antipseudomonal antibiotics within three days of admission. Eligible patients were randomly divided into derivation and validation cohorts. Predictors of in-hospital mortality were identified using multivariable logistic regression, and a prognostic score was developed. Among 13,340 patients, 2,511 (18.8%) died during hospitalization. Age ≥ 85 years, male sex, body mass index < 18.5 kg/m², Barthel Index < 70, impaired consciousness, poor Hugh-Jones classification, chronic heart failure, interstitial pneumonia, renal failure, and malignancy were independently associated with in-hospital mortality. The score showed similar discrimination in the derivation and validation cohorts, with AUCs of 0.650 and 0.652, respectively. This score may help identify older patients with aspiration pneumonia who remain at high risk of in-hospital mortality despite broad-spectrum antibiotic therapy.

INTRODUCTION

Pneumonia is one of the leading causes of death among older adults worldwide. According to the 2019 Global Burden of Disease report, which analyzed disease burden across 204 countries and territories, pneumonia caused 2.5 million deaths in 2019, including 1.2 million deaths among older adults [1]. Aspiration pneumonia is a pulmonary infection associated with the aspiration of oropharyngeal or upper gastrointestinal contents and is commonly related to decreased swallowing function [2, 3]. Age-related physiological changes, such as dysphagia, malnutrition, and prolonged bedridden status, have been reported as risk factors for aspiration pneumonia [4, 5]. Aspiration pneumonia accounts for an increasing proportion of pneumonia cases in older age groups [6]. Furthermore, the incidence and mortality of aspiration pneumonia have been shown to increase in regions with an aging population [7]. A systematic review reported that aspiration pneumonia was associated with higher risks of in-hospital and 30-day mortality than non-aspiration pneumonia [8].

Antibiotic therapy is the mainstay of pneumonia treatment, and the risk of drug-resistant pathogens should be considered when selecting antibiotics [9]. Reported risk factors for drug-resistant pathogens in pneumonia include prior isolation of drug-resistant organisms, hospitalization and intravenous antibiotic use within the previous 90 days, recent antibiotic exposure, tracheostomy, and mechanical ventilation [10]. Older adults often have these risk factors [11]. Therefore, broad-spectrum antibiotics are used in a considerable proportion of older patients with aspiration pneumonia. However, evidence that this strategy improves mortality in this population remains limited. Several studies have reported that broad-spectrum antibiotics did not improve mortality or were associated with an increased risk of drug-

resistant pathogens [12–14]. The development and clinical outcomes of infectious diseases, including pneumonia, are influenced by interactions among the pathogen, host, and environment [15].

Expanding the antibiotic spectrum can be regarded as an enhanced intervention targeting pathogen-related factors. In contrast, impaired swallowing function associated with aging and frailty is a host-related factor that may not be readily reversible. In such patients, further intensification of pathogen-directed treatment is unlikely to improve outcomes. Nevertheless, predictors of poor outcomes despite broad-spectrum antibiotic therapy have not been well characterized. With antimicrobial resistance posing an increasing global health threat, the prudent use of broad-spectrum antibiotics has become a key component of antimicrobial stewardship [16]. Predicting patients in whom broad-spectrum antibiotics are unlikely to improve prognosis may contribute to antimicrobial stewardship. This study aimed to develop a prognostic prediction model to identify older patients with aspiration pneumonia who remain at high risk of in-hospital mortality despite receiving broad-spectrum antibiotics, using the Diagnosis Procedure Combination (DPC) database [17], a nationwide database covering most acute care hospitals in Japan.

RESULTS

Data on 97,763 patients aged ≥ 65 years who were hospitalized with aspiration pneumonia from January 2018 to December 2018 were extracted from the DPC database. Second or subsequent hospitalizations during the study period, deaths within three days of admission, patients without antibiotic therapy within three days of admission, those who received antibiotics without antipseudomonal activity within three days of admission, and those with missing data were excluded. After these exclusions, 13,340 patients who received antipseudomonal antibiotics within three days of admission were included in the final analysis (Fig. 1).

In the overall cohort, the mean age was 84.5 years, and 5,699 patients (42.7%) were female. The mean body mass index was 19.0 kg/m², and the mean Barthel Index was 16.2. Impaired consciousness was observed in 731 patients (5.5%). Oxygen administration was required in 9,566 patients (71.7%), and mechanical ventilation was performed in 647 patients (4.9%). A total of 2,511 patients (18.8%) died during hospitalization. The eligible patients were randomly divided into derivation and validation cohorts, comprising 9,346 and 3,994 patients, respectively. No statistically significant differences were observed between the two cohorts (Table 1). Univariable analyses in the derivation cohort identified several factors associated with in-hospital mortality, including patient characteristics, clinical status at admission, and comorbidities (Table 2). Multivariable logistic regression analysis identified age ≥ 85 years, male sex, body mass index < 18.5 kg/m², Barthel Index < 70, impaired consciousness, poor Hugh-Jones classification, chronic heart failure, interstitial pneumonia, renal failure, and malignancy as factors independently associated with in-hospital mortality (Table 3). Based on these factors, a prognostic model for predicting in-hospital mortality was developed (Table 4). Three points were assigned to Barthel Index < 70, poor Hugh-Jones classification, and interstitial pneumonia. Two points were assigned to male sex, body mass index < 18.5 kg/m², impaired consciousness, chronic heart failure, renal failure,

and malignancy. One point was assigned to age ≥ 85 years. These scores were assigned based on the ratios of the corresponding β coefficients to the smallest β coefficient. The AUCs for in-hospital mortality were 0.650 in the derivation cohort and 0.652 in the validation cohort (Fig. 2). The number of patients and the corresponding in-hospital mortality rate were plotted for each prognostic score (Fig. 3).

Table 1
Baseline characteristics of patients in derivation cohort and validation cohort.

Age (years)	**Overall**	**Derivation cohort**	**Validation cohort**	***p* value**
	(n = 13340)	**(n = 9346)**	**(n = 3994)**	
	84.5 ± 7.8	**84.4 ± 7.8**	**84.7 ± 7.7**	**0.058**
Sex (female)	5699 (42.7)	4025 (43.1)	1674 (41.9)	0.217
BMI (kg/m^2)	19.0 ± 3.7	19.0 ± 3.7	19.0 ± 3.7	0.978
Barthel Index	16.2 ± 30.1	16.2 ± 30.0	16.4 ± 30.3	0.699
Current/past smoker	3252 (24.4)	2283 (24.4)	969 (24.3)	0.838
Impaired consciousness	731 (5.5)	528 (5.6)	203 (5.1)	0.188
Hugh-Jones classification				0.917
1	572 (4.3)	405 (4.3)	167 (4.2)	
2	634 (4.8)	433 (4.6)	201 (5.0)	
3	633 (4.7)	439 (4.7)	194 (4.9)	
4	1432 (10.7)	1001 (10.7)	431 (10.8)	
5	2630 (19.7)	1853 (19.8)	777 (19.5)	
unclassifiable	7439 (55.8)	5215 (55.8)	2224 (55.7)	
Chronic heart failure	2022 (15.2)	1399 (15.0)	623 (15.6)	0.353
Dementia	3773 (28.3)	2642 (28.3)	1131 (28.3)	0.954
Interstitial pneumonia	215 (1.6)	161 (1.7)	54 (1.4)	0.119
COPD	394 (3.0)	278 (3.0)	116 (2.9)	0.826
Bronchiectasis	141 (1.1)	94 (1.0)	47 (1.2)	0.376
Collagen disease	226 (1.7)	161 (1.7)	65 (1.6)	0.696
Liver failure	246 (1.8)	166 (1.8)	80 (2.0)	0.372
Diabetes	2126 (15.9)	1472 (15.8)	654 (16.4)	0.367
Hemiplegia or paraplegia	55 (0.4)	37 (0.4)	18 (0.5)	0.651
Renal failure	824 (6.2)	554 (5.9)	270 (6.8)	0.067
Malignancy	1339 (10.0)	958 (10.3)	381 (9.5)	0.211
Values are presented as the mean ± standard deviation or number (%).				

Age (years)	**Overall (n = 13340)**	**Derivation cohort (n = 9346)**	**Validation cohort (n = 3994)**	***p* value**
	84.5 ± 7.8	**84.4 ± 7.8**	**84.7 ± 7.7**	**0.058**
HIV/AIDS	1 (< 0.1)	1 (< 0.1)	0 (0)	1.000
Cerebrovascular disease	2979 (22.3)	2120 (22.7)	859 (21.5)	0.135
Oxygen administration	9566 (71.7)	6694 (71.6)	2872 (71.9)	0.739
Mechanical ventilation	647 (4.9)	458 (4.9)	189 (4.7)	0.678
In-hospital death	2511 (18.8)	1747 (18.7)	764 (19.1)	0.555
Values are presented as the mean ± standard deviation or number (%).				

Abbreviations: AIDS, acquired immunodeficiency syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

Table 2
Univariate analysis of factors associated with in-hospital mortality in the derivation cohort.

Age ≧ 85 (years)	**Survivors (n = 7599)**	**Non-survivors (n = 1747)**	***p* value**
	4012 (52.8)	**1014 (58.0)**	**< 0.001**
Sex (male)	4194 (55.2)	1127 (64.5)	< 0.001
BMI < 18.5 (kg/m^2)	3559 (46.8)	1021 (58.4)	< 0.001
Barthel Index < 70	6762 (89.0)	1670 (95.6)	< 0.001
Current/past smoker	1823 (24.0)	460 (26.3)	0.040
Impaired consciousness	378 (5.0)	150 (8.6)	< 0.001
Poor Hugh-Jones classification	6826 (89.9)	1679 (96.1)	< 0.001
Chronic heart failure	1056 (13.9)	343 (19.6)	< 0.001
Dementia	2180 (28.7)	462 (26.4)	0.061
Interstitial pneumonia	115 (1.5)	46 (2.6)	0.001
COPD	224 (2.9)	54 (3.1)	0.751
Bronchiectasis	73 (1.0)	21 (1.2)	0.362
Collagen disease	132 (1.7)	29 (1.7)	0.823
Liver failure	135 (1.8)	31 (1.8)	0.995
Diabetes	1211 (15.9)	261 (14.9)	0.303
Hemiplegia or paraplegia	27 (0.4)	10 (0.6)	0.193
Renal failure	415 (5.5)	139 (8.0)	< 0.001
Malignancy	719 (9.5)	239 (13.7)	< 0.001
HIV/AIDS	1 (< 0.1)	0 (0)	1.000
Cerebrovascular disease	1740 (22.9)	380 (21.8)	0.302

Values are presented as number (%).

Abbreviations: AIDS, acquired immunodeficiency syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

Table 3
Multivariate analysis of factors associated with in-hospital mortality in the derivation cohort.

Age ≧ 85 (years)	**β**	**OR**	**95% CI**	***p* value**
	0.263	**1.300**	**1.163–1.454**	**< 0.001**
Sex (male)	0.523	1.687	1.493–1.906	< 0.001
BMI < 18.5 (kg/m^2)	0.449	1.567	1.406–1.745	< 0.001
Barthel Index < 70	0.870	2.386	1.855–3.070	< 0.001
Current/past smoker	-0.016	0.985	0.862–1.125	0.819
Impaired consciousness	0.590	1.804	1.475–2.207	< 0.001
Poor Hugh-Jones classification	0.777	2.175	1.672–2.830	< 0.001
Chronic heart failure	0.425	1.529	1.329–1.759	< 0.001
Interstitial pneumonia	0.681	1.976	1.382–2.824	< 0.001
Renal failure	0.430	1.537	1.251–1.888	< 0.001
Malignancy	0.550	1.733	1.467–2.046	< 0.001
Abbreviations: BMI, body mass index.				

Table 4
Prognostic scoring model for predicting in-hospital mortality. Abbreviations: BMI, body mass index.

Barthel Index < 70	**Score**
	3
Poor Hugh-Jones classification	3
Interstitial pneumonia	3
Male	2
BMI < 18.5 (kg/m^2)	2
Impaired consciousness	2
Chronic heart failure	2
Renal failure	2
Malignancy	2
Age ≧ 85 (years)	1

Abbreviations: BMI, body mass index.

DISCUSSION

In this nationwide cohort study of 13,340 older patients with aspiration pneumonia who received broad-spectrum antibiotics, impaired activities of daily living, host vulnerability, and comorbidities at admission were independently associated with in-hospital mortality. Among these factors, Barthel Index < 70, poor Hugh-Jones classification, and interstitial pneumonia each had an odds ratio of approximately 2.0 or greater for in-hospital mortality, suggesting that these factors were strongly associated with increased in-hospital mortality. Male sex, body mass index < 18.5 kg/m², impaired consciousness, chronic heart failure, renal failure, malignancy, and age ≥ 85 years were also significantly associated with increased in-hospital mortality. A scoring system based only on patient status at admission may help predict in-hospital mortality risk, with mortality rates increasing according to the score.

The Pneumonia Severity Index (PSI) [18] and CURB-65 [19] are representative prognostic models for pneumonia, and their clinical utility is widely recognized. However, the predictive performance of these scores has been shown to decline in older adults aged ≥ 65 years, particularly in very old patients aged ≥ 85 years [20]. Several studies have also investigated prognostic prediction specifically in older patients with pneumonia. In a study of older patients with severe community-acquired pneumonia, a prediction model for in-hospital mortality was developed, in which age, vasopressor use, chronic kidney disease, neutrophil count, platelet count, and blood urea nitrogen were included as risk factors [21]. Yoshimatsu

et al. conducted a retrospective observational study of patients aged ≥ 75 years with pneumonia. Although mortality was higher among patients diagnosed with aspiration pneumonia, the authors concluded that frailty, age, and cardiopulmonary comorbidities, rather than aspiration pneumonia itself, were associated with poor outcomes in multivariable analysis [22]. In addition, a long-term prognostic study of patients with aspiration pneumonia reported that male sex, low body mass index, hypoalbuminemia, anemia, and mechanical ventilation were independently associated with 1-year and 5-year mortality [23]. In the present study, which was restricted to older patients with aspiration pneumonia who received broad-spectrum antibiotics, age, sex, host vulnerability, and comorbidities at admission were identified as factors associated with prognosis. These findings are consistent with previous reports. Notably, measures of host vulnerability, such as the Barthel Index and Hugh-Jones classification, were more strongly associated with mortality than other risk factors. These findings suggest that, in older patients with aspiration pneumonia, host-related factors may have a greater influence on prognosis, and that the prognostic benefit of broad-spectrum antibiotic therapy may be limited.

Broad-spectrum antibiotics are generally administered when drug-resistant pathogens are suspected to be the causative organisms. However, even when drug-resistant organisms are isolated from respiratory specimens, such as sputum, methods to clearly distinguish true infection from colonization have not been fully established. Therefore, it should be considered that organisms isolated from sputum may not necessarily represent the causative pathogens. In a retrospective cohort study of patients with community-acquired pneumonia in whom *Pseudomonas aeruginosa* was isolated from sputum, with a median age of 85 years, cases that improved without antipseudomonal antibiotics were defined as colonization, whereas those that improved after switching to antipseudomonal antibiotics were defined as infection. Based on this definition, 113 of 130 patients were classified as having colonization [24]. Similar findings were reported in an observational study of patients with community-acquired pneumonia or healthcare-associated pneumonia who received antibiotic therapy. In this study, ESBL-producing bacteria were isolated from sputum cultures. The mean age of the patients was 84.1 years, and none received initial antibiotic therapy active against the isolated ESBL-producing bacteria. Nevertheless, 13 of the 15 patients improved with initial antibiotic therapy alone [25]. Although the evidence from these retrospective, small-scale studies is limited, their findings suggest that resistant organisms isolated from sputum, particularly in older patients, should be interpreted cautiously rather than being immediately regarded as causative pathogens. If colonizing organisms are regarded as causative pathogens, the use of broad-spectrum antibiotics may lead to unnecessary exposure. Exposure to broad-spectrum antibiotics has been suggested to be associated with an increased risk of *Clostridioides difficile* infection and antimicrobial resistance [26, 27]. Such adverse consequences may harm patients and potentially contribute to poor outcomes.

The main strength of this study is the large-scale analysis using a nationwide database, which may enhance the generalizability of the findings to older patients hospitalized with aspiration pneumonia. However, several limitations should be acknowledged. First, the DPC database provided limited clinical information, and data on vital signs, laboratory findings, radiographic findings, and microbiological test results were unavailable. For example, the PSI includes physical findings such as body temperature,

pulse rate, and respiratory rate; laboratory findings such as arterial pH, blood urea nitrogen, serum sodium, glucose, and hematocrit; and radiographic findings such as the presence of pleural effusion [18]. The lack of these variables may have reduced the predictive performance of the model. Indeed, the AUC of the proposed prediction model was modest at 0.652, which may partly reflect this limitation. In addition, microbiological test results were unavailable, and the proportion of patients with drug-resistant organisms detected in respiratory specimens was unknown. Furthermore, the diagnostic basis for aspiration pneumonia and comorbidities could not be confirmed because diagnoses were identified using ICD-10 codes. Second, information on the reasons for antibiotic selection, dosage, treatment duration, antibiotic changes, and concomitant medications was not considered. These differences may have influenced patient outcomes. Third, the retrospective cohort design limited our ability to establish causal relationships between the identified predictors and in-hospital mortality. In addition, antipseudomonal antibiotics were selected based on the attending physicians' clinical judgment, and selection bias may have remained. Finally, although internal validation was performed by randomly dividing patients into derivation and validation cohorts, external validation using a dataset other than the DPC database was not conducted. Therefore, further evaluation is needed to assess the generalizability of the model. Accordingly, this score should not be used as a stand-alone tool for determining treatment strategies, but should be interpreted as a supportive indicator for stratifying patients who remain at risk of poor outcomes despite receiving broad-spectrum antibiotics. In conclusion, host-related factors at admission, including impaired activities of daily living, reduced exercise tolerance, low body mass index, impaired consciousness, and comorbidities, were independently associated with in-hospital mortality among older patients with aspiration pneumonia who received broad-spectrum antibiotics. The prognostic score developed using these factors may help identify patients who remain at high risk of in-hospital mortality despite receiving broad-spectrum antibiotics. In frail older patients with aspiration pneumonia, expansion of the antibiotic spectrum alone may have limited prognostic benefit.

METHODS

Data source

This study used nationwide inpatient data from acute care hospitals in Japan obtained from the DPC database. This database includes the following information: age, sex, height and weight, diagnoses, comorbidities at admission coded according to the International Classification of Diseases 10th Revision (ICD-10), state of consciousness assessed by the Japan Coma Scale, Barthel Index, smoking history, Hugh-Jones classification, emergency transport, in-hospital procedures and medications, length of hospital stay, and discharge status. The present study used the same source database as our previous study [28] but addressed a distinct research question. Specifically, this analysis was restricted to older patients with aspiration pneumonia who received antipseudomonal antibiotics within three days of admission and focused on developing and validating a prognostic prediction model for in-hospital mortality. This study was approved by the Ethics Committee of the Faculty of Medicine, Oita University (approval no. 2764, approval date: 22 March 2024), and was conducted in accordance with the

Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study. Information regarding the study was posted in the hospital.

Study population

Data were extracted for patients aged ≥ 65 years who were hospitalized with aspiration pneumonia, defined by the ICD-10 code J690, between January and December 2018. We excluded second or subsequent hospitalizations during the study period, patients who died within three days of admission, those who did not receive antibiotic therapy within three days of admission, those who received antibiotics without antipseudomonal activity within three days of admission, and those with missing data. After these exclusions, patients who received antipseudomonal antibiotics within three days of admission were included in this study.

Data collection

Patient characteristics at admission were collected, including age, sex, body mass index, Barthel Index, smoking history, state of consciousness evaluated by the Japan Coma Scale, and dyspnea severity assessed using the Hugh-Jones classification. Comorbidities at admission included chronic heart failure, dementia, interstitial pneumonia, chronic obstructive pulmonary disease, bronchiectasis, collagen disease, liver failure, diabetes, hemiplegia or paraplegia, renal failure, malignancy, acquired immunodeficiency syndrome/human immunodeficiency virus, and cerebrovascular disease. These comorbidities were selected with reference to the Charlson Comorbidity Index, which is used to assess mortality risk according to comorbid conditions [29, 30]. Antibiotics administered during hospitalization were identified based on those listed in the Japanese Respiratory Society Guidelines for the Management of Pneumonia in Adults 2017 [31]. The collected antibiotics included penicillins, such as sulbactam/ampicillin, piperacillin (PIPC), and tazobactam/piperacillin (TAZ/PIPC); cephalosporins, such as ceftriaxone, cefotaxime, ceftazidime (CAZ), cefepime (CFPM), cefozopran (CZOP), and cefpirome (CPR); macrolides, such as azithromycin; carbapenems, such as imipenem/cilastatin (IPM/CS), meropenem (MEPM), doripenem (DRPM), and biapenem (BIPM); quinolones, such as levofloxacin (LVFX), ciprofloxacin (CPFX), and pazufloxacin mesylate (PZFX); tetracyclines, such as minocycline; oxazolidinones, such as linezolid; glycopeptides, such as vancomycin and teicoplanin; aminoglycosides, such as gentamicin (GM), amikacin (AMK), tobramycin (TOB), and arbekacin; lincomycins, such as clindamycin; and nitroimidazoles, such as metronidazole. Antipseudomonal antibiotics were defined as PIPC, TAZ/PIPC, CAZ, CFPM, CZOP, CPR, IPM/CS, MEPM, DRPM, BIPM, LVFX, CPFX, PZFX, GM, AMK, and TOB. In-hospital procedures, including oxygen administration and mechanical ventilation, were also collected.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 25 (SPSS, IBM, Armonk, NY, USA). Eligible patients were randomly divided into derivation and validation cohorts at a 7:3 ratio using random numbers. This ratio was selected based on previous studies [21, 32, 33]. Patient characteristics, comorbidities, in-hospital procedures, and in-hospital mortality were compared between the two cohorts using univariable analyses. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate, and continuous variables were analyzed using the t-test. Variables were categorized for the development of the scoring model. Body mass index was classified using a cutoff of 18.5 kg/m², according to the World Health Organization definition of underweight [34]. Impaired consciousness was defined as a Japan Coma Scale score of ≥ 100. The Hugh-Jones classification was grouped into grades I–II and III–V, because grade III or higher represents a clinically meaningful threshold indicating limitation in level-ground walking and has been associated with increased mortality risk in a previous DPC study of patients with pneumonia [35]. In the present study, poor Hugh-Jones classification was defined as grade III or higher, or unclassifiable status. For the Barthel Index, a cutoff value of 70 was used based on a previous DPC study of patients with pneumonia [36].

In the derivation cohort, multivariable logistic regression analysis was performed to identify factors associated with in-hospital mortality. Variables that were statistically significant in the univariable analyses and considered clinically relevant were included as candidate predictors in the multivariable model. A prognostic scoring model was developed based on the estimated β coefficients of the identified factors. The score assigned to each factor/category was calculated based on its ratio to the smallest β coefficient. The area under the receiver operating characteristic curve (AUC) of the scoring model was calculated in both the derivation and validation cohorts, and in-hospital mortality rates were assessed according to the score. The *p*-values < 0.05 indicated statistically significant differences.

Declarations

Competing interests

All authors declare that there are no competing interests in connection with this article.

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Author Contribution

R.K., A.H., H.S., S.O., D.Y., K.F., and K.K. substantially contributed to the study conceptualization, material preparation, data collection, and analysis. Further, R.K. and K.K. substantially contributed to manuscript drafting. All authors have read and agreed to the published version of the manuscript.

Data Availability

The data analyzed in this study were obtained from the Japanese Diagnosis Procedure Combination database under a data-use agreement and are not publicly available. Owing to restrictions imposed by the data provider and the need to protect patient confidentiality, the authors are not permitted to share the individual-level data with third parties. Researchers interested in accessing the data should contact the corresponding author, and access may be considered subject to approval by the relevant data provider and completion of the required data-use agreement. The aggregated data supporting the findings of this study are available within the article.

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Figures

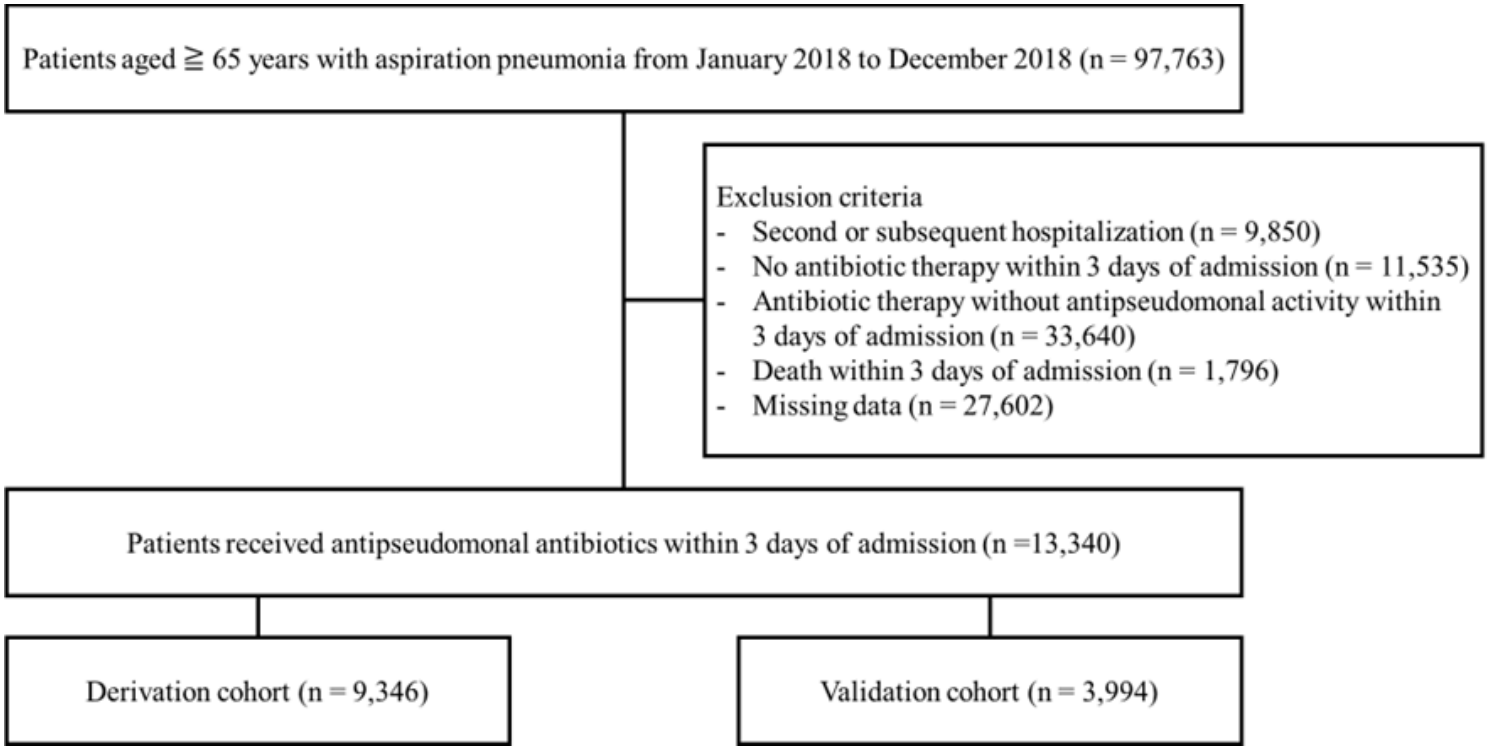


Figure 1

Flow chart of the patient selection process.

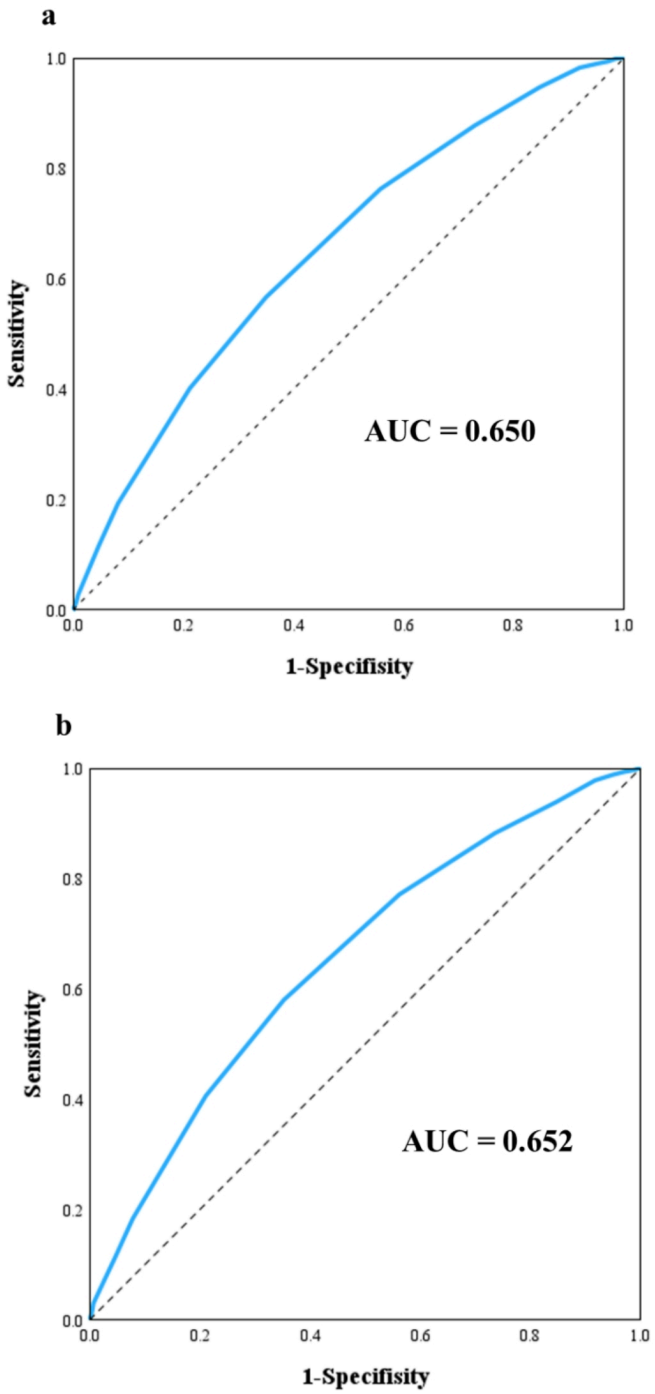


Figure 2

(a) The ROC curve for derivation cohort. (**b)** The ROC curve for validation cohort.

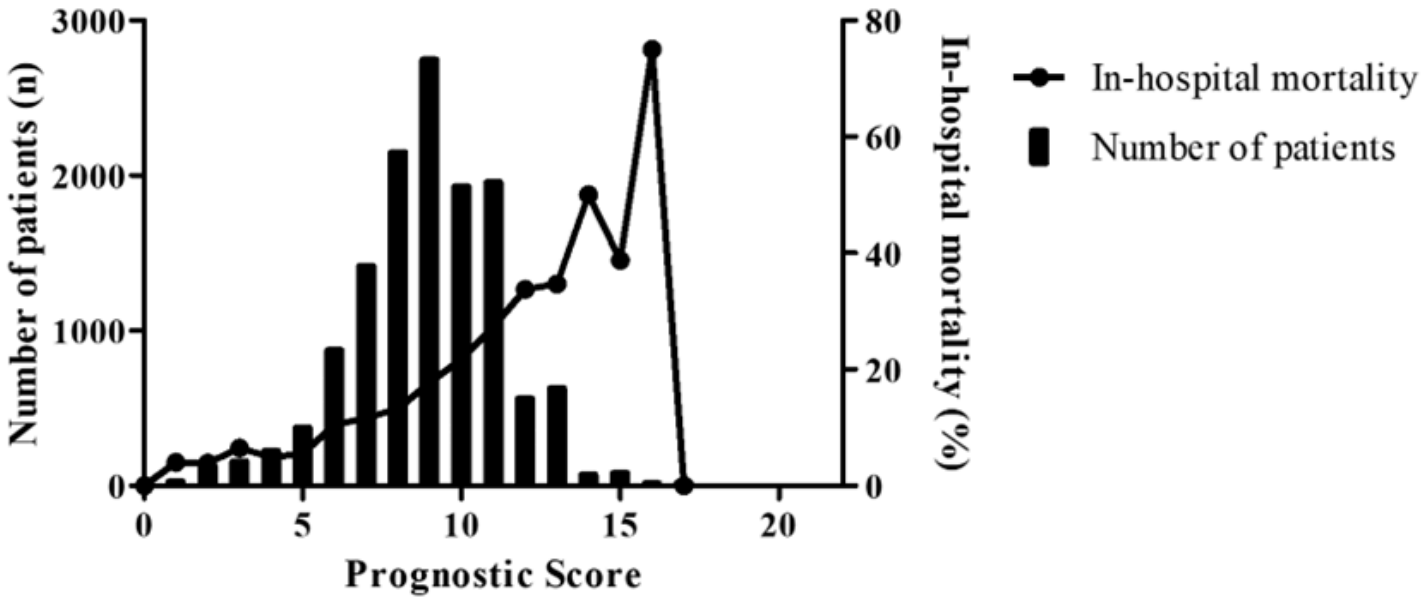


Figure 3

Number of patients and in-hospital mortality rate according to the prognostic score in validation cohort.